IN THE CLAIMS

The claims are as follows:

1. (Original) A method to enhance recombinant adeno-associated virus (rAAV) transduction of a mammalian cell, comprising: contacting the mammalian cell with at least one rAAV and at least two agents in an amount effective to additively or synergistically enhance rAAV transduction.

2. (Original) The method of claim 1 wherein the rAAV comprises a marker gene or a selectable gene.

3. (Original) The method of claim 1 further comprising contacting the cell with an agent that alters single strand to double strand rAAV genome conversion.

4. (Original) The method of claim 1 further comprising contacting the cell with an agent that alters cellular uptake of rAAV.

5. (Original) The method of claim 1 wherein the agents enhance transduction by at least 2 fold relative to transduction of a corresponding mammalian cell contacted with the rAAV and one of the agents or transduction of a corresponding mammalian cell contacted with the at least one rAAV but not contacted with the agents.

6. (Original) The method of claim 1 wherein the agents enhance transduction by at least 4 fold relative to transduction of a corresponding mammalian cell contacted with the rAAV and one of the agents or transduction of a corresponding mammalian cell contacted with the at least one rAAV but not contacted with the agents.

7. (Original) The method of claim 1 wherein the agents enhance transduction by at least 10 fold relative to transduction of a corresponding mammalian cell contacted with the

rAAV and one of the agents or transduction of a corresponding mammalian cell contacted with the at least one rAAV but not contacted with the agents.

8. (Original) The method of claim 1 wherein one of the agents is a chemotherapeutic, a lipid lowering agent, an antibiotic or a food additive.

9. (Original) The method of claim 1 wherein one rAAV comprises a first recombinant DNA molecule comprising linked:

i) a first DNA segment comprising a 5' inverted terminal repeat (ITR) of AAV;

ii) a second DNA segment comprising a heterologous DNA; and

iii) a third DNA segment comprising a 3' ITR of AAV.

10. (Original) The method of claim 9 further comprising a second rAAV comprising a second recombinant DNA molecule comprising linked:

i) a first DNA segment comprising a 5' ITR of AAV, and

ii) a second DNA segment comprising a heterologous DNA which has sequences that are different than the sequences in the second DNA segment of the first recombinant DNA molecule; and

iii) a third DNA segment comprising a 3' ITR of AAV.

11. (Original) The method of claim 10 wherein the second DNA segment of the first recombinant DNA molecule comprises a portion of an open reading frame for a gene product, optionally operably linked to at least one transcriptional regulatory element, and a splice donor site 3' to the portion of the open reading frame, and wherein the second DNA segment of the second recombinant DNA molecule comprises a splice acceptor site 5' to the remainder of an open reading frame, which together with the second DNA segment of the first recombinant DNA molecule encodes a functional gene product.

12. (Original) The method of claim 11 wherein the transcriptional regulatory element is a promoter.

13. (Original) The method of claim 11 wherein the transcriptional regulatory element is an enhancer.

14. (Original) The method of claim 10 wherein the second DNA segment of the first recombinant DNA molecule comprises an enhancer and the second DNA segment of the second recombinant DNA molecule comprises an open reading frame encoding a functional gene product.

15. (Original) The method of claim 10 wherein the second DNA segment of the first recombinant DNA molecule comprises a promoter and the second DNA segment of the second recombinant DNA molecule comprises an open reading frame encoding a functional gene product.

16. (Original) The method of claim 1 wherein the cell is a lung cell, an epithelial cell, a liver cell, a muscle cell, a hematopoietic cell, a heart cell, or a neuronal cell.

17. (Original) The method of claim 11, 14 or 15 wherein the expression of the functional gene product is enhanced.

18. (Original) The method of claim 9 wherein the second DNA segment encodes a functional gene product.

19. (Original) The method of claim 11, 14, 15 or 18 wherein the functional gene product is a therapeutic peptide or polypeptide or a prophylactic peptide or polypeptide.

20. (Original) The method of claim 19 wherein the functional polypeptide is cystic fibrosis transmembrane conductance regulator, β-globin, γ-globin, tyrosine hydroxylase, glucocerebrosidase, aryl sulfatase A, factor VIII, dystrophin or erythropoietin.

21. (Original) The method of claim 1 wherein one of the agents is epoxomicin, doxorubicin, doxil, daunorubicin, idarubicin, epirubicin, aclarubicin camptothecin, simvastatin, tannic acid, cisplatin, LLnL or Z-LLL.

22. (Original) The method of claim 1 wherein the cell is a human cell, canine cell, murine cell, rat cell or rabbit cell.

23. (Original) The method of claim 1 wherein the cell is contacted with at least one agent before the cell is contacted with the virus.

24. (Original) The method of claim 1 wherein the cell is contacted with the virus before the cell is contacted with at least one agent.

25. (Original) The method of claim 1 wherein at least one of the agents modulates microfilaments or microtubules.

26. (Original) The method of claim 1 wherein at least one of the agents modulates rAAV endocytosis.

27. (Original) The method of claim 1 wherein at least one of the agents modulates rAAV trafficking in the cell.

28. (Original) The method of claim 1 wherein at least one of the agents modulates rAAV processing in the cell.

29. (Original) The method of claim 1 wherein at least one of the agents modulates rAAV nucleic acid degradation in the cell.

30. (Original) The method of claim 1 wherein at least one of the agents modulates rAAV protein degradation in the cell.

31. (Original) The method of claim 1 wherein at least one of the agents modulates rAAV transport to the nucleus.

32. (Original) The method of claim 1 wherein at least one of the agents modulates viral genome transport to the nucleus.

33. (Original) A method to inhibit or treat a condition associated with aberrant expression of an endogenous gene product, comprising: contacting a mammal at risk of or having the condition, with an effective amount of at least one agent that enhances AAV transduction and an effective amount at least one rAAV comprising a transgene encoding at least a portion of a functional gene product, the expression of which in the mammal inhibits or treats at least one symptom of the condition, wherein the agent is a chemotherapeutic, a lipid lowering agent, an antibiotic or a food additive.

34. (Original) The method of claim 33 wherein the aberrant expression is the lack of or reduced expression of the endogenous gene product.

35. (Original) The method of claim 33 wherein one rAAV comprises a first recombinant DNA molecule comprising linked:

iv) a first DNA segment comprising a 5' ITR of AAV;

v) a second DNA segment comprising a heterologous DNA; and

vi) a third DNA segment comprising a 3' ITR of AAV.

36. (Original) The method of claim 35 further comprising a second rAAV comprises a second recombinant DNA molecule comprising linked:

ii) a first DNA segment comprising a 5' ITR of AAV, and

ii) a second DNA segment comprising a heterologous DNA which has sequences which are different than the sequences in the second DNA segment of the first recombinant DNA molecule; and

iii) a third DNA segment comprising a 3' ITR of AAV.

37. (Original) The method of claim 36 wherein the second DNA segment of the first recombinant DNA molecule comprises a portion of an open reading frame for a gene product, optionally linked to a transcriptional regulatory element, and a splice donor site 3' to the portion of the open reading frame, wherein the second DNA segment of the second recombinant DNA molecule comprises a splice acceptor site 5' to the remainder of an open reading frame, which together with the second DNA segment of the first recombinant DNA molecule encodes a functional gene product.

38. (Original) The method of claim 37 wherein the transcriptional regulatory element is a promoter.

39. (Original) The method of claim 36 wherein the second DNA segment of the first recombinant DNA molecule comprises an enhancer and the second DNA segment of the second recombinant DNA molecule comprises an open reading frame encoding a functional gene product.

40. (Original) The method of claim 36 wherein the second DNA segment of the first recombinant DNA molecule comprises a promoter and the second DNA segment of the second recombinant DNA molecule comprises an open reading frame encoding a functional gene product.

41. (Original) The method of claim 33 wherein the expression of the transgene is enhanced.

42. (Original) The method of claim 33 wherein the trangene encodes cystic fibrosis transmembrane conductance regulator, β-globin, γ-globin, tyrosine hydroxylase, glucocerebrosidase, aryl sulfatase A, factor VIII, dystrophin or erythropoietin.

43. (Original) A method to enhance rAAV transduction of a mammalian cell, comprising: contacting the mammalian cell with at least one rAAV and at least one agent that alters rAAV endocytosis, rAAV trafficking or processing in intracellular compartments, viral nucleic acid or protein degradation, nuclear transport of virus or viral genome, effective to enhance rAAV transduction, with the proviso that the agent is not an inhibitor of proteosome proteolytic activity.

44. (Original) The method of claim 43 wherein the rAAV comprises a marker gene or a selectable gene.

45. (Original) The method of claim 43 further comprising contacting the cell with an agent that alters single strand to double strand rAAV genome conversion.

46. (Original) The method of claim 43 wherein further comprising contacting the cell with an agent that alters cellular uptake of rAAV.

47. (Original) The method of claim 43 wherein one of the agents is a chemotherapeutic, a lipid lowering agent, an antibiotic or a food additive.

48. (Original) The method of claim 43 wherein the cell is a lung cell, an epithelial cell, a liver cell, a heart cell, a hematopoietic cell, a muscle cell or a neuronal cell.

49. (Original) The method of claim 43 wherein the rAAV expresses a therapeutic or prophylactic gene product.

50. (Original) The method of claim 43 wherein the cell is a human cell, canine cell, murine cell, rat cell or rabbit cell.

51. (Original) The method of claim 43 wherein at least one agent modulates microfilaments or microtubules.

52. (Original) The method of claim 43 wherein at least one agent modulates rAAV endocytosis.

53. (Original) The method of claim 43 wherein at least one agent modulates rAAV trafficking in the cell.

54. (Original) The method of claim 43 wherein at least one agent modulates rAAV processing in the cell.

55. (Original) The method of claim 43 wherein at least one agent modulates rAAV nucleic acid degradation in the cell.

56. (Original) The method of claim 43 wherein at least one agent modulates rAAV protein degradation in the cell.

57. (Original) The method of claim 43 wherein at least one agent modulates rAAV transport to the nucleus.

58. (Original) The method of claim 43 wherein at least one agent modulates viral genome transport to the nucleus.

59. (Original) The method of claim 43 wherein at least one agent modulates subcellular localization of proteosomes.

60. (Original) The method of claim 33 or 43 wherein at least one agent is epoxomicin, doxorubicin, doxil, daunorubicin, idarubicin, epirubicin, aclarubicin, simvastatin or tannic acid.